Taurine transporter, TAUT, is significantly down-regulated in photoexposed human skin

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INTRODUCTION

Ageing causes the skin to be more fragile with clinical features such as loss of elasticity and severe dryness [1]. These features occur due to deterioration of the skin structure and function which could be linked to changes in fundamental cell volume regulatory mechanisms. It is known that the effects of intrinsic ageing, which is genetically predetermined, can be enhanced or accelerated due to external factors (extrinsic ageing) [2,3]. Cellular water homeostasis is vital to an organisms survival especially in the skin which acts as a barrier to water loss. The importance of this has been previously highlighted where excessive loss of water (TEWL) can be fatal, for example, premature babies where the skin barrier is not fully formed [4]. Skin barrier function is also disrupted by environmental exposure such as UV. Cell volume regulatory mechanisms involve the transport of organic osmolytes. These are organic compounds which not only maintain cellular water content but can also act as antioxidants and assist in protein stabilisation to counteract damage [5,6].

Therefore, we aimed to characterise organic osmolyte transporter expression in human skin. We also investigated how these transporter proteins may be altered with intrinsic and extrinsic ageing. To further dissect the effects of UV, we evaluated the osmolyte transporters in the skin pre- and post-SSR exposure. With this, we aim to further our understanding of the role of organic osmolytes in the skin and begin to decipher the molecular controls behind cellular homeostasis.

EXPERIMENTAL DESIGN

In the first study, 4mm skin biopsies were collected from photoprotected buttock and photoexposed forearm of young (18-30 years; n=5) and aged (>65 year; n=6) healthy volunteers. In a second cohort, healthy volunteers (18-30 years; n=5) were subjected to acute solar-simulated radiation (SSR; 8xSED) at a photoprotected site. 4mm biopsies were taken at baseline (unirradiated) and +1, +3 and +72 hours post-irradiation. All samples were embedded in OCT compound and sectioned at 7µm for carrying out immunofluorescence microscopy. Protein expression of BGT-1, HMIT and TAUT was analysed in young versus aged, photoprotected and photoexposed skin. TAUT protein expression was also analysed in SSR-exposed skin. Statistical analysis was carried out using GraphPad Prism 7.0 to assess changes in average protein expression. A p value of 0.05 was considered as significant.

RESULTS

Figure 3 | The protein expression of the taurine transporter, TAUT, is downregulated in photoageing

(a-d) TAUT, taurine transporter, is expressed throughout the epidermis of human skin as a gradient with highest expression in the stratum granulosum and lowest expression in the basal layer. This expression pattern is also occurs in the photoprotected buttock skin and photoexposed forearm skin of young and aged subjects. (e-g) TAUT protein expression was measured in the whole epidermis, suprabasal layers and basal layer. TAUT is significantly downregulated in the epidermis, suprabasal layers and basal layer of aged photoexposed skin compared to aged photoprotected skin. (f) TAUT protein expression is also significantly downregulated in the suprabasal layer of aged photoexposed skin compared to young photoexposed skin.

Figure 4 | TAUT protein expression is significantly downregulated at 72 hours post-SSR exposure

(a-d) Healthy subjects were exposed to acute solar simulated radiation (SSR) on photoprotected buttock skin and samples taken at baseline (0 hours), then +1, +3 and +72 hours after SSR exposure. TAUT protein expression was measured in the whole epidermis, suprabasal layers and basal layer. (e-g) TAUT protein expression did not change at +1 or +3 hours after SSR compared to baseline. However, TAUT is significantly downregulated at +72 hours post-SSR exposure in the epidermis, suprabasal layers and basal layer when compared to baseline. Data presented ±SEM (n=5). Scale bars = 20µm

CONCLUSIONS

For the first time ,we have characterised the specific expression patterns of the organic osmolytes transporters BGT-1, HMIT and TAUT in human skin. The unique expression patterns of these transporters suggest each osmolyte could have a defined function in the skin.

Although there was no change in BGT-1 or HMIT protein expression with intrinsic or extrinsic ageing, our results demonstrate that TAUT protein expression is significantly downregulated in the epidermis with photoageing. Further investigation in to the effect of UV on TAUT protein expression revealed downregulation at 72 hours post-SSR exposure.

This shows for the first time that chronic UV results in a decrease in TAUT protein, indicating that taurine transporter may be fundamental in the pathophysiology of skin photoageing. Therefore, taurine could be considered as a novel therapeutic target. Further investigation into the molecular mechanisms behind the controls of TAUT function and taurine accumulation into cells will reveal how this could be targeted.

References

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